

## REMARKS

### Preliminary Remarks

With this response, applicants amend claim 44 to recite steps of “providing a library of *in vitro* mutagenized nucleic acid from an existing antibody coding sequence” and “wherein the specific binding pair members are Fab antibody fragments.” The written support for these amendments can be found throughout the specification as filed, including Examples 30, 38 and 45.

With this response, applicants add two new claims 61 and 62. The written support for claims 61 and 62 can be found throughout specification as filed, including at lines 23 through 32 of page 15.

### Patentability Arguments

#### A. The Rejections of Claims 44, 47-48 Under 35 U.S.C. § 102(a or e) Should be

#### Withdrawn

##### 1. Rejection over US Patent 5,837,500 to Ladner (“Ladner US”)

At page 3 of the Office action, the Examiner rejected claims 44 and 47-48 allegedly as being anticipated by Ladner US under 35 U.S.C. § 102(e). Applicants respectfully traverse the rejection in view of the foregoing amendments and following remarks.

With this response, applicants amend claim 44 so that the claim recites the positive step of “providing a library of *in vitro* mutagenized nucleic acid from an existing antibody coding sequence.” Applicants also amend claim 44 so that the claim recites that the specific binding pair member is a Fab antibody fragment.

At page 3 of the office action, the Examiner characterizes Ladner US as disclosing a method of obtaining a nucleic acid encoding a proteinaceous binding domain that binds a predetermined target. The Examiner further alleges that the proteinaceous binding domain of

Ladner US is identical to “the member of specific binding pair of the instant claims.” This assertion is in error because Ladner US does not disclose display on filamentous bacteriophage multi-chain proteins such as Fab antibody fragments. Further, in column 19, Ladner US teaches that its binding domain is preferably small (under 40 residues), while the instantly claimed Fab fragment is about 400 amino acids long.

In conclusion, Ladner US cannot anticipate claims 44, 47-48 of the instant application because it fails to disclose a binding domain comprising more than one polypeptide or a method of obtaining a member of a specific binding pair wherein the specific binding pair member is a Fab fragment. Therefore, rejection over Ladner US under 35 U.S.C. §102(e) may be properly withdrawn.

**2. Rejection over US patent application 2002/0150881 to Ladner  
 (“Ladner US application”)**

At page 4 of the office action, the Examiner rejected claims 44, 46-48, 51-52 allegedly as being anticipated by Ladner US application under 35 U.S.C. § 102(a or e). Applicants respectfully traverse this rejection in view of the foregoing amendments and following remarks.

Claims 46, 51 and 52 are canceled with this response. Further, applicants amend herewith claim 44 so that the claim positively recites the step of “providing a library of *in vitro* mutagenized nucleic acid from an existing antibody coding sequence.” Applicants amend claim 44 further so that the amended claim is directed to the specific binding pair members that are Fab antibody fragments.

At page 5 of the office action, the Examiner alleges that the Ladner US application anticipates the instant claims because “the antibody variable domains of Ladner US application claims read on the instant claim single chain antibodies or scFV.” However, as stated above the

claims as presently amended are directed to a method of obtaining a member of a specific binding pair wherein the specific binding member is a Fab antibody fragment. Ladner US application does not disclose display on filamentous bacteriophage of a multi-chain polypeptide such as a Fab fragment of an antibody.

In conclusion, because Ladner US application does not disclose display on filamentous bacteriophage of any multi-chain polypeptides such as Fab antibody fragments, the rejection of the instant claims over Ladner US application under 35 U.S.C. §§102(a) or (e) maybe properly withdrawn.

### **3. Rejection over US patent 5,427,908 to Dower (Dower US)**

At page 6 of the office action, the Examiner rejected claims 44, 47-48 allegedly as being anticipated by Dower US under 35 U.S.C. §102(e). Applicants respectfully traverse the rejection in view of the foregoing amendments and following remarks.

At page 6 of the office action, the Examiner alleges that Dower US anticipates instant claims because it teaches filamentous bacteriophage library encoding antibody fragments which read on the instant claim binding domains of immunoglobulin. Dower US is concerned with cloning of natural libraries and nowhere discloses the step of “providing a library of *in vitro* mutagenized nucleic acid from an existing antibody coding sequence,” as recited in the instant claims.

Dower US fails to teach mutating a nucleic acid encoding any specific binding pair member, let alone an antibody Fab fragment, to produce a genetically diverse population as is called for by the present claims. Rather, Dower US refers to cloning such genes from a nucleotide library - i.e., prepare a naturally diverse library then look to clone a single protein that binds a particular ligand.

Specifically, Dower US states:

“The protein for which the DNA is enriched and cloned according to the present invention is typically an antibody or fragment thereof, but may also be any protein which may be cloned from a nucleotide library. In addition to antibodies, such proteins may include, for example, growth hormones, interferons, interleukins, hormones, enzymes, zymogens, etc. Proteins which may be cloned are those for which specific binding partners (e.g., antigen or hapten when the desired protein is an antibody) have been identified.”

In conclusion, because Dower US fails to teach a library of *in vitro* mutagenized nucleic acid from an existing antibody coding sequence, Dower US cannot anticipate claims 44, 47-48 of the instant application. Therefore, rejection over Dower US under 35 U.S.C. §102 (e) may be properly withdrawn.

**B. Rejection of claims 44, 46-48 and 51-52 under Judicially Created Doctrine of Obviousness-type Double Patenting over co-owned US patent 5,969,108 Should be Withdrawn**

At page 7 of the office action, the Examiner rejected claims 44, 46-48 and 51-52 under judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-59 of co-owned US patent 5,969,108. Claims 46, 51 and 52 are canceled with this response. Furthermore, applicants submit herewith a terminal disclaimer which obviates the double patenting rejection by disclaiming the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of the co-owned patent. Therefore, the rejection may be properly withdrawn.

**C. Rejection of claims 44, 46-48 and 51-52 under Judicially Created Doctrine of Provisional Obviousness-type Double Patenting over co-pending US application 10/803,653 Should be Withdrawn**

At page 8 of the office action, the Examiner provisionally rejected claims 44, 46-48 and 51-52 as being unpatentable over claims 1-5 of co-pending application 10/803,653. At page eight of the office action, the Examiner states: “although the conflicting claims are not identical,

they are not patentably distinct because . . . the binding molecule of the reference reads on the scFv and immunoglobulin domain of the instant claims.” Claims 46, 51 and 52 are canceled with this response. Claim 44 as presently amended is directed to a method of obtaining a member of a specific binding pair wherein the specific binding member is an antibody Fab fragment and not a scFv.

Nevertheless, applicants submit herewith a terminal disclaimer that obviates the provisional double patenting rejection by disclaiming the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on the co-owned US application 10/803,653. Therefore, the rejection of claims 44, 47-48 under the judicially created doctrine of provisional obviousness-type double patenting over claims 1-5 of US application 10/803,653 may be properly withdrawn.

**D. Rejection of claims 44, 46-48 and 51-52 under Judicially Created Doctrine of  
Provisional Obviousness-type Double Patenting over co-pending US  
application 10/803,622 Should be Withdrawn**

At page 8 of the office action, the Examiner provisionally rejected claims 44, 46-48 and 51-52 as being unpatentable over claims 1-17 of co-pending application 10/803,622. At page eight of the office action, the Examiner states: “although the conflicting claims are not identical, they are not patentably distinct because . . . the binding molecule of [co-pending application 10/803,622] consists of dAb, which reads on the scFv and immunoglobulin domain of the instant claims.” Claims 46, 51 and 52 are canceled with this response. Instant claim 44 as presently amended is directed to a method of obtaining a member of a specific binding pair wherein the specific binding member is an antibody Fab fragment and not a dAb or a scFv.

Nevertheless, applicants submit herewith a terminal disclaimer that obviates the provisional double patenting rejection by disclaiming the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on the co-owned US application 10/803,622.

Therefore, the rejection of claims 44, 47-48 under the judicially created doctrine of provisional obviousness-type double patenting over claims 1-17 of US application 10/803,622 may be properly withdrawn.

### **Conclusion**

In view of the above amendments and remarks, applicants respectfully submit that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the (312) 595-1408.

Respectfully submitted,

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